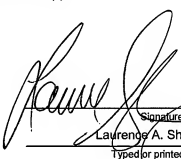


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PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number (Optional) 10913.0003-00000	
		Application Number 10/568,098	Filed June 20, 2006
		First Named Inventor Steffen GOLETZ	
		Art Unit 1633	Examiner Maria Leavitt
<p>Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.</p> <p>This request is being filed with a notice of appeal.</p> <p>The review is requested for the reason(s) stated on the attached sheet(s). Note: No more than five (5) pages may be provided.</p>			
<p>I am the</p> <p><input type="checkbox"/> applicant/inventor.</p> <p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)</p> <p><input checked="" type="checkbox"/> attorney or agent of record. Registration number 61,169</p> <p><input type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34</p>		<p> Signature Laurence A. Shumway Typed or printed name 617.452.1689 Telephone number December 23, 2009 Date</p>	
<p>NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below".</p>			
<p><input checked="" type="checkbox"/> *Total of 1 forms are submitted.</p>			

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)	
)	
Steffen Goletz et al.)	Group Art Unit: 1633
)	
Application No.: 10/568,098)	Examiner: Leavitt, Maria
)	
Filed: June 20, 2006)	Confirmation No.: 8158
)	
For: TUMOR CELL LINES AND USES)	
THEREOF)	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

PRE-APPEAL BRIEF REQUEST FOR REVIEW

In reply to the Final Office Action mailed July 23, 2009, and further to the Advisory Action mailed October 7, 2009, and Examiner's Interview Summary mailed October 28, 2009, Applicants respectfully submit this Pre-Appeal Brief Request for Review in conjunction with a Notice of Appeal under 37 C.F.R. §41.31, Appeal fee payment, and form PTO/SB/33. Applicants request this Pre-Appeal Brief Conference in accordance with the guidelines set forth in the Official Gazette Notice of July 12, 2005. The period for filing this request was extended to December 23, 2009 by the previously filed Petition for Extension of Time of two-months and payment of the required fee.

Upon entry of the previously filed amendment, claims 1, 3, 5, 6, 11, 12, 23, and 24 will be pending and under examination.

Clear error is present in the rejections of claims 1, 3, 5, 6, 11, 12, 23, and 24. Claim 1 stands rejected under 35 U.S.C. § 102(b) over Ichiyama, *Kareitigaku Kenkyusho*

Zasshi 51(3,4):93-110 (2000)(*Ichiyama*), in view of *Benoist et al.*, *Immunol. Lett.* 34:45-56 (1992)(*Benoist*), and *Karsten et al.*, *Cancer Res.* 58:2541-49 (1998)(*Karsten*). Claims 1, 5, 6, 11, 12, and 24 stand rejected under 35 U.S.C. § 103(a) over *Ichiyama*, in view of *Hinoda et al.*, *J. Clin. Lab. Anal.* 7:100-04 (1993), abstract (*Hinoda*), in view of *Benoist* and *Karsten*, and further in view of U.S. Patent No. 7,268,120 to Horton, *et al.* (*Horton*). Finally, claims 1 and 23 were also rejected under 35 U.S.C. § 103(a) over *Ichiyama* in view of *Benoist*, *Karsten*, and further in view of *Springer*, *J. Mol. Med.* 75:594-602 (1997) (*Springer*).

The claimed invention: The claims are directed to a cell line that expresses three antigens on its cell surface—Thomsen-Friedenreich antigen (TF), mucin 1 (MUC1), and glycophorin—as well as, *inter alia*, particular deposited cell lines, transformed cells, and compositions containing the cells.

Basis of the rejection: The outstanding rejections under 35 U.S.C. §§ 102(b) and 103(a) are all based on the Examiner's mistaken assertion that TF is inherently present in the MUC-1-transformed K562-derived cells of *Ichiyama*. *Benoist* has been cited as alleged evidence that the K562-derived cells in *Ichiyama* express glycophorin, while *Karsten*—a study on synthetic MUC1 peptides engineered to contain TF—has been cited as alleged evidence that MUC1 contains glycans containing the core-1 disaccharide. The Examiner seems to believe that *any* larger carbohydrate structure that contains a core-1 disaccharide "expresses TF."

Factual Defects of the rejections: The rejections all rely on the same scientific error: the Examiner's unsupported contention that the core-1 disaccharide is the same thing as TF antigen, irrespective of whether the core-1 is exposed. In response to the

first Office Action, Applicants provided the Examiner with explicit, direct evidence from the application that K562 cells (used in *Ichiyama*) do not express TF. See page 20 of the Response filed April 27, 2009, referencing, *inter alia*, Figure 1 (K562 cells negative for TF expression), Table 2 (TF can only be detected in K562 cells after neuraminidase treatment), and pages 10 and 50 in the application ("TF which is absent on K562..."). In the second Office Action, the Examiner maintained the rejection, yet acknowledged that "access to the TF glycotope in MUC1 and/or glycophorin [in K562 cells] was inhibited by the presence of terminal sialic acids...." See page 9 of the Office Action mailed July 23, 2009. In response, Applicants pointed out that the term "TF" corresponds to an *exposed* core-1 (Gal β 1-3GalNAc) motif—not more complex carbohydrate structures that simply contain the core-1 disaccharide along with additional moieties, such as sialic acid. See, e.g., pages 9-10 of the Response filed September 23, 2009, referencing page 6 of the specification ("expression of the inner core sugar Core-1, *which equals TF when exposed...*") (emphasis added); see also *Karsten*, cited in the rejections, at 2541, right column ("[t]hese [synthetic] glycopeptides carry Gal β 1-3GalNAc α (TF antigen)..."). Applicants further pointed out that "expression" of the antigens recited in the claims relies on the cell's own synthesis machinery and offered to amend claim 1 to state that the cell "synthesizes and expresses" the recited antigens and make this implicit feature of the claimed cells more clear. See page 11 of the Response filed September 23, 2009. Despite the arguments and evidence discussed above, the Examiner maintained all the outstanding rejections in an Advisory Action mailed October 7, 2009, stating that "the recitation of the TF in claim 1 is broadly but reasonably interpreted as exposed or hidden as part of larger sugar core-1 molecule [sic], naked, further glycosylated,

elongated with any degree of sialylation.” Advisory Action at 9. The Examiner, however, failed to provide any basis to support this vacuous definition of the term “TF.”

Legal defects of the rejection: In an Examiner interview on October 23, 2009, Applicants’ representative suggested two possible clarifying amendments to claim 1 (and analogously to claims 3 and 11) to state that **1)** the cells expressing TF, MUC1 and glycoporphin, “*synthesize and express*” these antigens, and **2)** “*wherein the TF is exposed.*” The Examiner indicated that these amendments would make the claims free of the art—even though the amendments do not introduce additional limitations into the claims or additional distinctions over the art for the reasons discussed above—*i.e.*, cells that express an antigen with synthesize and express the antigen, and TF antigen corresponds to *exposed* core-1. Accordingly, since the proposed amended claims discussed in the interview were free of the art, and the amendments simply emphasized differences with the art already present in the claims, then the pending claims must also be free of the art. To hold otherwise is clear legal error.

It is also legal error for the Examiner to rely solely on unsubstantiated allegations that the core-1 disaccharide is the same as TF antigen, even when core-1 is not exposed. This statement, in addition to being unsupported is contradicted by the evidence of record. Accordingly, the Examiner has not made a *prima facie* case of unpatentability over the cited art.

In sum, maintaining the rejections of claims 1, 3, 5, 6, 11, 12, 23, and 24 would be clear error. The Office has acknowledged that amendments that simply emphasize *existing* distinctions of the claims over the prior art obviate the rejections. Accordingly, the rejections have been overcome and should be withdrawn. If the Office disputes the

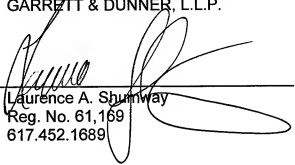
patentability of the claims on new grounds, then the Office should issue a new, non-final Office Action to afford Applicants a meaningful opportunity to respond.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: December 23, 2009

By: _____


Laurence A. Shumway
Reg. No. 61,169
617.452.1689